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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/753,313
Filing Date: December 29, 2000
Appellant(s): CASTILLO ET AL.

PATRICK MICHAEL DWYER
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11 September 2006 appealing from the Office action mailed 05 January 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

JP 10-245342	MITSUI NORIN INC.	09-1998
4,892,883	CHATTERJEE et al.	01-1990

SELKOE, D. "Alzheimer's Disease: Genes, Proteins, and Therapy" Physiological Reviews. Vol. 81, No. 2 (April 2001), pages 741-766.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

Claims 4, 5, 10, and 28-32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the previous Office action which are restated below.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly recited claim limitations "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" (claims 4, 28, and 31) and "produced by process have the steps of (1) water extraction, using water that is not boiling" (claim 31) are deemed new matter as the Examiner could not find adequate support for these limitations within the instant disclosure.

Claim Rejections - 35 USC § 102

Claims 4, 5, and 28-31 stand rejected under 35 U.S.C. 102(b) as being anticipated by Mitsui Norin (JP 10-245342), or by Takami et al. (JP 10-175858) for the reasons set forth in the previous Office action which are restated below.

Mitsui Norin teaches the administration (e.g., in oral dosage form) of a therapeutically effective amount of epicatechin (which is a naturally-occurring compound extracted from green tea and, thus, reads upon a green tea extract) as well as green tea extract (per se), to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells and, thus, reduce the toxicity of beta-amyloid protein (see entire English translation of this JP patent) - please note that beta-amyloid protein is medically well known to be responsible for amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence. [Further, as previously discussed, Applicants readily admit that "Alzheimer's disease is characterized by the accumulation of ... beta-amyloid protein or A*B*, in a fibrillar form, existing as extracellular amyloid plaques and as amyloid with the wall of cerebral blood vessels. Fibrillar A*B* amyloid deposition in Alzheimer's disease is believed to be detrimental to the patient and eventually leads to toxicity and neuronal cell death characteristic hallmarks of Alzheimer's disease. Accumulating evidence implicates amyloid as a major causative factor of Alzheimer's disease pathogenesis" - see page 1, lines 12-18 of the instant specification - accordingly, the claimed functional effect would inherently occur upon the oral administration of an effective amount of green tea extract, as taught by the cited reference.]

Takami et al. teach the administration (e.g., in the form of a pharmaceutical tablet, capsule, etc; or within a consumable drink or food, etc) of a pharmacologically effective amount

of a green tea extract (which is produced via warm or hot water extraction; e.g., TEAFURAN 30) containing epicatechin therein, or a component thereof - such as epicatechin, including to someone suffering from Alzheimer's disease brought about by toxicity of beta amyloid protein. See entire computer-generated English translation of the JP patent. Please again note that claimed functional effect would inherently occur upon the oral administration of an effective amount of green tea extract, as taught by the cited reference. Please also note that such an amount would inherently be in an amount to provide the claimed functional effect.

It is reemphasized that the above reference methods would inherently provide the functional effects instant claimed - i.e., would inherently treat/disrupt amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon oral consumption of a therapeutically effective amount such a green tea extract since amyloid fibril formation, deposition, accumulation, aggregation and/or persistence is inherently present in Alzheimer's patients (see, e.g., page 1, lines 12-18 of the instant specification - as discussed above; in addition, also see the review article by Selkoe including, e.g., page 743 under the heading *Neuritic Plaques* with respect to the inherent presence of amyloid fibrils in Alzheimer's patients).

Therefore, each of the cited references is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

Claims 4, 5, 10, and 28-32 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsui Norin and Takami et al. (JP 10-175858), in view of Chatterjee et al.

(US 4,892,883) and the admitted state of the art for the reasons set forth in the previous Office action which are restated and expanded upon below.

The primary references are relied upon for the reasons discussed *supra*. Neither of these references expressly teach the further inclusion of the herbal agents instantly recited in claim 10.

Chatterjee et al. beneficially disclose that administration of *Ginkgo biloba* is useful in the therapy of Alzheimer's disease (see, e.g., col 7, lines 13-39).

It would have been obvious to employ a therapeutically effective amount of green tea extract - such as beneficially taught by Mitsui Norin and Takami et al., for administering to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells based upon the beneficial teachings provided therein. [As noted above and in previous Office actions, the reference methods would intrinsically provide the functional effects instant claimed - i.e., would intrinsically treat/disrupt amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon such oral consumption.]

It would also have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine (and orally administer) green tea extract with *Ginkgo biloba* (for treating Alzheimer's disease) for the following reasons. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is beneficially taught to be useful for the same purpose (e.g., treating Alzheimer's disease) in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Sussman, 1943 C.D. 518; In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445;

169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

With respect to the USC 112, first paragraph rejection, Appellants' arguments have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicants argue that Example I of the instant specification recites "extracted in 1 ml of distilled water" and, thus, persons of skill in the art would take this statement in the context of its attendant disclosure to mean that the water was not boiling, else it would have been so specified. However, as previously discussed, the specification does not preclude the use of boiling water and, thus, this negative limitation is still considered to be new matter. Further, there is no appreciation within the instant specification teachings for using non-boiled water in preparing the instantly disclosed green tea extract, including with regard to criticality and/or unexpected results achieved thereby. Concerning the limitation "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" (as recited in claims 4, 28, and 31), Applicants argue that the entire thrust of the disclosure is directed to amyloid inhibition by administering the therapeutic amount of substance. However, amyloid inhibition does not

necessarily or directly correlate to providing the limitation "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" and, thus, this limitation is still deemed to be new matter.

With respect to the USC 102 rejections of record, Appellants' arguments have been carefully considered but are not deemed to be persuasive of error in the rejections. Appellants argue that the claims (including all independent claims) require selection of a therapeutic substance that can only be green tea, green tea leaves, or green tea extract, and that none of the claims require the use of epicatechin. However, as discussed in the art rejections above, each of the references relied upon by the Examiner within the USC 102 rejections (i.e., the Mitsui Norin and Takami et al. references) teach the use of green tea extract as a therapeutic agent in treating Alzheimer's disease. With respect to the Mitsui Norin reference, please note that tea polyphenols (as well as epicatechin) are naturally-occurring compounds found in tea (such as green tea) and, therefore, read upon a green tea extract (since they are, in fact, extractable from green tea including from green tea leaves, such as by boiling- as discussed in the Mitsui Norin reference: see, e.g., page 6, paragraph [0027] of the full English translation of record for this document).

Regarding the Mitsui Norin, Appellants further argue that this reference teaches narrowly that certain kinds of nerve cell toxicity that is supposedly caused by beta-amyloid protein, can possibly be reduced with tea polyphenols, and that the Examiner is reading into the Mitsui Norin reference something more than it actually contains, when he states that it teaches giving green tea extract "to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to deposition of beta-amyloid protein on brain nerve cells" so that the

toxicity of beta-amyloid protein is reduced; and in fact, Mitsui Norin makes no reference whatever to any of these processes. However, as discussed *supra*, the Mitsui Norin reference expressly teaches the administration (e.g., in oral dosage form) of a therapeutically effective amount of epicatechin (which is a naturally-occurring compound extracted from green tea and, thus, reads upon a green tea extract) as well as green tea extract (e.g., tea polyphenols derived/extracted from boiled green tea leaves), to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells and, thus, reduce the toxicity of beta-amyloid (see, e.g., pages 2-3, paragraphs [0001] - [0006] of the full English translation of record for this document). In addition, please note that the Mitsui Norin reference further discloses that "Alzheimer's disease and senile dementia of Alzheimer are morphologically degenerative diseases ... Their noticeable pathological findings are (1) a senile plaque in the cerebral cortex or hippocampal cell, and the deposition of beta-amyloid protein, and (2) changing the neuroofibril" (see paragraph [0002] of the full English translation of this document).

Regarding the Takami reference, Appellants further argue that Takami makes no mention of fibril formation at all; that this reference only teaches narrowly that a certain kind of active oxygen toxicity can be reduced by disclosed extracts of green tea containing various catechins; and that nothing beyond a passing reference is said about Alzheimer's disease, and certainly nothing about treating amyloid fibrils. However, as discussed *supra*, Takami et al. teach the administration (e.g., in the form of a pharmaceutical tablet, capsule, etc; or within a consumable drink or food, etc) of a pharmacologically effective amount of a green tea extract (which is produced via warm or hot water extraction; e.g., TEAFURAN 30) containing epicatechin therein,

or an extracted component thereof - such as epicatechin, including to someone suffering from Alzheimer's disease brought about by toxicity of beta amyloid protein. See entire computer-generated English translation of the JP patent including page 2, paragraph [0002] of the full computer-assisted English translation of record for this document).

Accordingly, for the reasons fully set forth above, the functional effects instant claimed (i.e., treat/disrupt amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence) would inherently occur upon oral consumption of a therapeutically effective amount of the reference green tea extracts by a subject suffering from Alzheimer's disease since amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence is inherently present in Alzheimer's patients. Appellants present several references which purportedly indicate that the underlying mechanisms of *AB*-mediated neurotoxicity are still controversial and, thus, further refute anything that might be regarded as a "necessary" suggestion that inhibition of beta amyloid fibril formation, deposition, accumulation, and/or persistence; and that no necessary inferences can be drawn from the cited studies pertaining to neuronal cell death or active oxygen reduction as to beta amyloid fibrillogenesis. However, the Examiner maintains that by treating a subject suffering from Alzheimer's disease with either of the reference green tea extracts (as reasonably taught therein), beta amyloid fibril formation, deposition, accumulation, and/or persistence would inherently occur (for the reasons discussed *supra*). Otherwise, as discussed in the previous Office action and above, the instant invention would not work as claimed/disclosed, especially since in each case green tea extract (as taught by each of the cited references and by the instant disclosure) is being provided to the same patient population (i.e., a subject suffering from Alzheimer's disease). In other words, Applicants appear to be arguing patentability based

upon discovering (and claiming) an underlying functional effect concerning how green tea extract works with respect to treating a subject suffering from Alzheimer's disease. However, as discussed above, this underlying functional effect (i.e., treating/disrupting amyloid fibril formation, deposition, aggregation, and/or persistence) would inherently occur in an Alzheimer's patient being administered a therapeutically effective amount of such a green tea extract - including those disclosed by the cited prior art references.

Appellants further argue that the Examiner simply offers no objective support for his assertion that the claimed underlying functional effect would inherently occur upon oral administration of an effective amount of green tea extract, as taught by the cited references. However, the Examiner did, in fact, provide objective evidence to support this assertion in the previous Office action and above - that is, the Examiner provided objective evidence within the USC 102 rejections above via pointing to the admitted state of the art as disclosed within background section of the instant specification, as well as a reference by Selkoe (which was made of record) therein. More fully, the instant specification expressly discloses (admits) within the Background section of the invention: "Alzheimer's disease is characterized by the accumulation of a 39-43 amino acid peptide termed the beta-amyloid protein or *AB* in a fibrillar form, existing as extracellular amyloid plaques and as amyloid within the walls of cerebral blood vessels. Fibrillar A*B* amyloid deposition in Alzheimer's disease is believed to be detrimental to the patient and eventually leads to toxicity and neuronal cell death characteristic hallmarks of Alzheimer's disease. Accumulating evidence implicates amyloid as a major causative factor of Alzheimer's disease pathogenesis" (see page 1, lines 12-18 of the instant specification); and the Selkoe reference expressly teaches "Neuritic plaques, one of the two diagnostic brain lesions

observed in Alzheimer's original patient, are microscopic foci of extracellular amyloid deposition and associated axonal and dendritic injury, generally found in large numbers in the limbic and association cortices ... Such plaques contain extracellular deposits of amyloid *B*-protein (*AB*) that occur principally in a filamentous form, i.e., as star-shaped masses of amyloid fibrils." (see Selkoe reference - page 743 under the heading *Neuritic Plaques*).

As such, the Patent Office has met the burden in showing that the invention defined by claims 4, 5, and 28-31 is anticipated over each of the cited references set forth in the USC 102 rejections above.

With respect to the USC 103 rejection of record, Appellants' arguments have been carefully considered but are not deemed to be persuasive of error in the rejection. Appellants argue that for the reasons discussed within their arguments over the USC 102 rejections, none of the cited references alone or in combination make obvious the combination of steps and substances instantly claimed including the limitations set forth in dependent claims 10, 30 and 32 (which further require the administration of a therapeutic quantity of one of the recited ingredients therein, which includes *Ginkgo biloba*). However, Appellants have argued and discussed the cited references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Appellants' claimed invention fails to patentably distinguish over the state of the art represented by the

references. Regarding claims 10, 30, and 32, Appellants also argue that the Examiner's supposition that any of the listed ingredients (recited in claims) are known in the art to be efficacious in treating amyloid fibrils remains unsupported. However, the Examiner would like to again point out it appeared to him, based upon the teachings of the instant specification, that the ingredients recited therein are admittedly well known in the art to function as such since none of the herbal agents recited in claims 10, 30, and 32 were actually tested in the instant Examples, and page 6, lines 14-20, of the instant specification merely states that they are amyloid inhibitory ingredients. Regardless, as discussed in the previous Office action and above, Chatterjee et al. beneficially disclose that administration of *Ginkgo biloba* is useful in the therapy of Alzheimer's disease (see, e.g., col 7, lines 13-39). Accordingly, the USC 103 rejection with respect to claims 10, 30, and 32 is deemed proper because, as discussed above, it is well known to be *prima facie* obvious to combine two or more ingredients each of which is beneficially taught to be useful for the same purpose - i.e., treating Alzheimer's disease, in order to form a third composition which is useful for the same purpose (as well as to actually use such a combination to treat Alzheimer's disease in a subject) - for the reasons fully set forth above under USC 103.

Appellants further argue that amended claim 4 recites two distinct method steps not disclosed in any cited reference - i.e., treating amyloid fibril formation, deposition, accumulation, aggregation and/or persistence in Alzheimer's disease and such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils; and that claim 28 includes an express recitation that the fibrils to be treated are already existing. However, as repeatedly discussed within the previous Office action and above, the oral consumption of green tea extract to a subject suffering from Alzheimer's disease, as reasonably disclosed by the two

primary references (including in combination), would intrinsically provide the functional effects instant claimed - i.e., would intrinsically treat/disrupt amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease - in which amyloid fibrils would already inherently exist (as evidence, again see, e.g., page 1, lines 12-18 of the instant specification, as well as the review article by Selkoe including, e.g., page 743 under the heading *Neuritic Plaques* with respect to the inherent presence of amyloid fibrils in Alzheimer's patients - as discussed fully above).

Appellants also argue that instant claim 31 (drawn to a method of using a product-by-process) requires that that the green tea extract be created by water extraction using water that is not boiling as well as removal of the fluid supernatant therefrom. However, as discussed in the previous Office action and above, with respect to the instantly claimed method of using a product-by-process (e.g., claim 31), please note that in product-by-process claims (including methods of using a product-by-process), "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 and/or 103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. Appellants have failed to objectively show an unobvious difference between the green tea extract products taught by the cited references and the claimed green tea extract product (including that used within the method of instant claim 31). That is, other than arguing that the Mitsui Norin reference uses boiling water in which the tea polyphenols are then separated therefrom via HPLC and, thus, is prepared by a different process that that recited in instant claim 31 (whereby the claimed steps comprise extraction of green tea with water that is not boiling, followed by separation and lyophilization of the supernatant from the water extraction), no objective evidence has been provided to show an unobvious difference

between the Mitsui Norin green tea extract and the green tea extract of claim 31, especially given that the instant specification further discloses using HPLC to prepare therapeutically effective amyloid inhibitory extract fractions from the lyophilized green tea water extract (see, e.g., page 10, line 35 - page 11, line 6; and page 11, line 29 - page 12, line 16 of the instant specification). In addition, please note that the Mitsui Norin reference also teaches that the green tea preparation can be made via freeze-drying (see, e.g., page 2, paragraph [0012], of the English translation of this document). Accordingly, the therapeutic green tea extract preparation disclosed by the Morin Norin reference is deemed to reasonably read upon the green tea extract product-by-process of instant claim 31. Regarding the Takami et al. reference (as discussed in the previous Office action and above), this reference expressly teaches that their water extract can be prepared via warm (thus, not boiling) or hot water extraction (paragraph [0010]) and then dried (which would inherently separate the supernatant therefrom). Accordingly, the therapeutic green tea extract preparation disclosed by Takami et al. is also deemed to reasonably read upon the green tea extract product-by-process of instant claim 31.

As such, the Patent Office has met the burden in showing that the invention defined by claims 4, 5, 10, and 28-32 is *prima facie* obvious over the combination of cited references within the USC 103 rejection above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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